Remarks

Amendments to the Claims

Claim 1 has been amended to recite that "increased levels [of a human endogenous MMTV-like subgroup 1 (HML-2) retrovirus encoded expression product in a test sample relative to a negative control sample] of at least 150% are indicative of prostate cancer." The specification supports this amendment at page 25, line 18: "The up-regulation [of an HML-2 encoded expression product in the test sample] relative to the control (100%) will usually be at least 150%."

Claim 13 has been amended to depend upon claim 2 in place of claim 11, canceled. This amendment merely addresses a formal matter.

None of these amendments introduce new matter.

The Rejection of Claims 1-3, 9-11, and 13-15 Under 35 U.S.C. § 112, second paragraph

Claims 1-3, 9-11, and 13-15 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite. Claim 11 was canceled in applicants' amendment filed February 5, 2005. Applicants respectfully traverse the rejection of independent claim 1 and dependent claims 2, 3, 9, 10, and 13-15.

A claim is definite if those skilled in the art would understand the scope of a claim when the claim is read in light of the specification. *North Am. Vaccine, Inc. v. American Cyanamid Co.*, 7 F.3d 1571 (Fed. Cir. 1993); *Miles Lab., Inc. v. Shandon, Inc.*, 997 F.2d 870 (Fed. Cir. 1993).

The Office Action asserts that the term "human endogenous MMTV-like subgroup 2 (HML-2)" is indefinite because it does not identify a structure required for diagnosis of prostate

cancer. Office Action at page 2, lines 14-15. One of skill in the art, however, would understand the *scope* of HML-2 as recited in the rejected claims.

At the time of the effective filing date of the application, December 7, 2000, HML-2 was a well known family of retroviruses to those of skill in the art. The specification discloses, "Because HML-2 is a well-recognized family, the skilled person will be able to determine without difficulty whether any particular endogenous retroviruses is or is not a HML-2." Page 37, lines 11-12. Thus, being well aware of the structure of members of the HML-2 family of retroviruses, one of skill in the art would have been able to determine the *scope* of the genus of HML-2.

The Patent Office asserts, however, that one of skill in the art's knowledge of structures of the genus of HML-2 retroviruses at the time the application was filed does not render the scope of the claims definite because it "does not address the problem with identifying which structures are critical for the claimed method." Office Action at page 2, lines 16-18. This assertion appears to concern whether the claims are operable across their full scope, *i.e.*, whether they are operable for any expression product of any HML-2 retrovirus. This assertion therefore appears to concern the enablement requirement of 35 U.S.C. § 112, *first* paragraph.[1] Enablement is not a requirement of 35 U.S.C. § 112, *second* paragraph.

Applicants respectfully request withdrawal of this rejection.

The Rejections of Claims 1-3, 9-11, and 13-15 Under 35 U.S.C. § 112, First Paragraph

Claims 1-3, 9-11, and 13-15 stand rejected under 35 U.S.C. § 112, first paragraph, as insufficiently described. Claim 11 was canceled in applicants' amendment filed February 5,

[1] This concern is addressed in the discussion of the enablement rejection, below.

2005. Applicants respectfully traverse the rejection of independent claim 1 and dependent claims 2, 3, 9, 10, and 13-15.

The Patent Office asserts that the claimed methods are not adequately described because

> the art indicates that HML-2 comprises a diverse group of retroelements having diverse structures at the nucleic acid level. The art has not correlated the occurrence with an increased HML-2 to any disease stage. HERV-K (HML-2) is expressed in normal tissue as well as well as cancerous tissue. Because the expression can occur in both cancerous and normal tissue an increase in expression will not correlate with a diagnosis of any kind of disease...Therefore, only the isolated polynucleotide sequences that have actually been correlated with prostate cancer meet the written description provision of 35 U.S.C. § 112, first paragraph.

Office Action at page 3, lines 6-20, citations omitted, emphasis in original. To expedite prosecution, claim 1 has been amended to recite that the method for diagnosing prostate cancer comprises a step of detecting increased levels "of at least 150%" of a HML-2 retrovirus encoded expression product in a patient prostate or blood sample relative to a negative control sample. The expression of HML-2 in normal and disease tissues does not disprove that an increase of at least 150% in expression levels of any HML-2 retrovirus encoded expression product in a patient prostate or blood sample relative to a negative control sample will indicate cancer. The Office Action does not provide evidence supporting a conclusion that any level of increased HML-2 retrovirus encoded expression products in a patient prostate or blood sample relative to a negative control sample will not indicate cancer.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991).

Information which is well known in the art need not be described in detail in the specification. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986).

One of skill in the art would reasonably conclude that applicants were in possession of the claimed invention. The claimed methods are for diagnosing prostate cancer. The specification discloses that the invention encompasses methods of diagnosing prostate cancer. The specification discloses, "The present invention relates to the diagnosis of cancer, particularly prostate cancer. In particular, it relates to a subgroup of human endogenous retroviruses (HERVs) which show up-regulated expression in tumors, particularly prostate tumors." Page 1, lines 11-13.

The claimed methods comprise a step of detecting increased levels of a HML-2 retrovirus encoded expression product in a patient prostate or blood sample relative to a negative control sample. One of skill in the art would readily recognize that applicants were in possession of each of the elements recited in this step of the claimed method. The specification discloses detecting increased levels of a HML-2 encoded expression product in a patient sample relative to a negative control sample. The specification discloses, "Higher levels of [HML-2] expression product relative to a negative control indicate that the patient from whom the sample was taken has, for example, prostate cancer." Page 24, lines 13-14. The specification also discloses that the patient sample in which the higher expression levels is detected is a prostate or blood sample. The specification discloses, "In general, therefore, the patient sample is a tissue sample (*e.g.*, a biopsy), preferably, a prostate sample (*e.g.*, a biopsy) or a blood sample." Page 3, lines 7-8.

Furthermore, the specification discloses that the sequences of HML-2 retroviruses, whose expression products are detected in the method, were well known in the art at the time of the effective filing date of the application, December 7, 2000. The specification explicitly teaches:

"Because HML-2 is a well-recognized family, the skilled person will be able to determine without difficulty whether any particular endogenous retroviruses is or is not a HML-2." Page 37, lines 11-12. The specification supports its assertion that HML-2 retroviruses were known in the art prior to its December 7, 2000 effective filing date. The specification teaches that:

> HERV isolates which are members of the HML-2 subgroup include HERV-K10 [137, 142], the 27 HML-2 viruses shown in Figure 4 of reference 147, HERV-K(C7) [148], HERV-K(II) [145], HERV-K(CH). Table 11 provides a list of all known members of the HML-2 subgroup of the HERV-K family as determined by searching the Double-Twist database containing all genomic contigs with the sequence AF074086 using the Smith-Waterman algorithm with the default parameters: open gap penalty = -20 and extension penalty = -5.

Page 35, lines 16-22. The specification references 31 published HML-2 retrovirus sequences that were known in the art prior to December 7, 2000 and describes an additional 28 HML-2 retrovirus sequences in Table 11. The specification supports the genus of HML-2 retroviruses by referencing 59 HML-2 retrovirus sequences.

Because the sequences of HML-2 retroviruses were known in the art, their RNA and polypeptide expression products also are easily recognized. Nonetheless, the specification provides numerous examples of sequences of HML-2 expression products including examples of: gag nucleotide sequences (page 16, lines 7-9), gag polypeptide sequences (page 16, lines 10-12), prt nucleotide sequences (page 16, lines 17-18), prt nucleotide sequences (page 16, lines 19-20), pol nucleotide sequences (page 16, lines 24-25), pol polypeptide sequences (page 16, lines 26-27), env nucleotide sequences (page 17, lines 4-5), env polypeptide sequences (page 17, lines 6-7), cORF nucleotide sequences (page 17, line 13), and cORF polypeptide sequences (page 17, line 14).

Finally, the claimed methods recite that increased levels of at least 150% are indicative of prostate cancer. Again, the specification describes applicants' invention such that the skilled artisan would recognize applicants were in possession of the claimed invention. The specification discloses, "The up-regulation relative to the control (100%) will usually be at least 150%..." Page 25, lines 18-19.

Thus, applicants describe each element of the methods encompassed by claims 1-3, 9, 10, and 13-15. One of skill in the art would recognize from the teachings of the specification that applicants were in possession of the claimed methods. The claims are adequately described.

Applicants respectfully request withdrawal of this rejection.

The Rejection of Claims 1-7, 9-11, and 13-15 Under 35 U.S.C. § 112, First Paragraph

Claims 1-7, 9-11, and 13-15 stand rejected under 35 U.S.C. § 112 first paragraph as not enabled. Claim 11 was canceled in applicants' amendment filed February 5, 2005. Applicants respectfully traverse the rejection of independent claim 1 and dependent claims 2, 3, 9, 10, and 13-15.

The enablement requirement sets forth that the specification must describe how to make and use the claimed invention. 35 U.S.C. § 112, ¶ 1. To satisfy the enablement requirement, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation'. *In re Wright,* 999 F.2d 1557, 1561 (Fed. Cir. 1993). Whenever the Patent Office rejects claims as not enabled, it must explain why it doubts the truth or accuracy of any statement in applicant's supporting disclosure and back up any assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. *In re Marzocchi*, 439 F.2d 220 (CCPA 1971).

The Office Action asserts that the claims are not enabled because it may be possible that an increase in a HML-2 retrovirus encoded expression product will not be indicative of prostate cancer. The Office Action asserts,

> HERV-K (HML-2) is expressed in normal tissue as well as cancerous tissue. Because the expression can occur in both cancerous and normal tissue an increase in expression will not correlate with a diagnosis of any kind of disease. A diagnosis could only be made with those sequences for which such a correlation has been established and would be limited to specific sequences.

Office Action at page 4, lines 12-18, citations omitted.

As discussed above, claim 1 has been amended to recite that for the method to diagnose prostate cancer comprises detecting increased levels of a HML-2 retrovirus encoded expression product in a patient prostate or blood sample relative to a negative control sample by "at least 150%." The mere fact that HML-2 retrovirus encoded expression products can be detected in cancerous and normal tissues would not lead one of skill in the art to reasonably conclude that detecting an increase of at least 150% of HML-2 expression products in a patient prostate or blood sample relative to a negative control sample is not indicative of prostate cancer. The Office Action does not provide any acceptable evidence or reasoning which is inconsistent with applicant's statements that detection of increased levels of HML-2 retrovirus encoded expression products in a prostate or blood sample relative to a negative control sample by at least 150% is indicative of prostate cancer.

One of skill in the art would accept applicant's statements that increased expression of any HML-2 expression product in a patient prostate or blood sample by at least 150% indicates prostate cancer. The specification discloses, at Table 6, results of DNA microarray analysis of expression of HERV-K RNA in thirteen patient tumor prostate vs. normal prostate samples. The

results of the microarray analysis show increased expression levels of HML-2 mRNA by greater than 150% in most prostate tumor samples relative to normal prostate samples. The specification also discloses, at Table 10, that HML-2 retrovirus expression products are upregulated in tumor tissue relative to non-tumor tissue of prostate cancer patients. The Patent Office has not made a *prima facie* case that the claims are not enabled.

Moreover, the claims are enabled because one of skill in the art would be able to make and use the method of claim 1, the only independent claim of the rejected claim set, without resorting to undue experimentation. Claim 1 comprises a single step of detecting an increase in expression of HML-2 retrovirus encoded expression products in a patient blood or prostate sample relative to a negative control sample. Increased levels of at least 150% are indicative of prostate cancer. One of skill in the art would be able to perform this step of the methods without resorting to undue experimentation. The specification teaches one of skill in the art how to detect HML-2 retrovirus encoded expression products. The specification teaches example methods of directly (page 9, line 27 to page 10, line 14) and indirectly (page 10, lines 15-22) detecting HML-2 encoded mRNA expression products. The specification also teaches hybridization conditions for an example method of directly detecting mRNA at page 12, lines 13-30. The specification further teaches example methods of directly (page 17, line 15 to page 18, line 22) and indirectly (page 18, lines 23-29) detecting the HML-2 encoded polypeptide expression products. The specification also teaches how to detect an increased level of HML-2 retrovirus encoded expression product in a patient prostate of blood sample relative to a negative control sample at page 24, line 7 to page 25, line 16.

One of skill in the art would be able to make and use at least the above-described techniques to detect any expression product of any HML-2 retrovirus. The specification

discloses that the sequences of HML-2 retroviruses were well-known in the art at the time the application was filed and references 59 such HML-2 retrovirus sequences. See the specification at page 35, lines 16-22 and Table 11.

Finally, one of skill in the art would be able to determine if the levels of expression of a HML-2 encoded expression product in a patient prostate or blood sample are increased at least 150% relative to a negative control sample. Methods of quantitating and comparing levels of expression products were well known in the art at the time the application was filed. One of skill in the art would be able to perform the step of detecting in the claimed methods.

One of skill in the art would not have to resort to undue experimentation to make and use the methods of diagnosing prostate cancer as claimed in claim 1, or dependent claims 2, 3, 9, 10, and 13-15. The claims are enabled.

Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,
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